J Cardiol 2006 May; 47(5) : 219–228

Hyperuricemia Associated With High Cardiac Event Rates in the Elderly With Chronic Heart Failure

Takeshi NIIZEKI, MD
Yasuchika TAKEISHI, MD, FJCC
Takanori ARIMOTO, MD
Hidenobu OKUYAMA, MD
Naoki NOZAKI, MD
Osamu HIRONO, MD
Yuichi TSUNODA, MD
Tetsu WATANABE, MD
Joji NITOBE, MD
Takehiko MIYASHITA, MD
Hiroki TAKAHASHI, MD
Yo KOYAMA, MD
Isao KUBOTA, MD, FJCC

Abstract

Objectives. Congestive heart failure (CHF) is the major cause of death and hospitalization in the elderly population. Simple markers that can be measured anywhere at low cost are necessary to identify patients at high risk. Recent studies have reported that hyperuricemia is a prognostic marker for CHF. However, it is not yet known whether serum levels of uric acid may provide prognostic information in the elderly population. Therefore, this study tried to identify the clinical characteristics of elderly CHF patients ($\geq$ 70 years) in our institution and to evaluate whether uric acid levels can effectively estimate the prognosis for elderly CHF patients.

Methods and Results. Uric acid levels were analyzed in 247 CHF patients, and patients were followed up for 451 $\pm$ 235 days (mean $\pm$ SD). Elderly CHF patients aged $\geq$ 70 years (123 patients) had higher rate of hypertension, lower current smoking rate and higher uric acid levels than those aged $<$ 70 years (124 patients). There were 72 cardiac events including cardiac deaths and readmissions for worsening CHF. Multivariate analysis with the Cox proportional hazard model showed that uric acid was the only independent predictor of cardiac events (hazard ratio 1.544, 95% confidence interval 1.215–2.582, $p < 0.0001$) in the elderly with CHF. The highest quartile of uric acid level was associated with the highest risk of cardiac events (a 4.45-fold compared to the lowest quartile). Kaplan-Meier analysis revealed that uric acid levels effectively risk stratified elderly CHF patients for cardiac events.

Conclusions. These findings suggest that measurement of uric acid levels in elderly CHF patients may add valuable prognostic information to predict cardiac events.

J Cardiol 2006 May ; 47(5) : 219–228

Key Words

■Heart failure (uric acid) ■Prognosis ■Elderly

山形大学医学部器官病態統御学講座 循環・呼吸・腎臓内科学分野 : 〒990–9585 山形県山形市飯田西2–2–2
Department of Cardiology, Pulmonology, and Nephrology, Yamagata University School of Medicine, Yamagata
Address for correspondence : TAKEISHI Y, MD, FJCC, Department of Cardiology, Pulmonology, and Nephrology, Yamagata University School of Medicine, Iida-Nishi 2–2–2, Yamagata, Yamagata 990–9585 ; E-mail : takeishi@med.id.yamagata-u.ac.jp
Manuscript received January 6, 2006 ; revised January 26, 2006 ; accepted February 7, 2006

INTRODUCTION

Chronic heart failure (CHF) is the leading cause of death and hospitalization among elderly patients, and the incidence of CHF increases with advancing age[1–5]. CHF is accompanied by various pathophysiological changes which trigger disease progression, and deterioration of ventricular function is still common in elderly patients with CHF[6,7]. Although the current therapy for CHF such as angiotensin-converting enzyme inhibitors and β-blockers can relieve symptoms and prolong life, the incidence, readmission rate and mortality are still increasing beacause of the aging of the population[8–12]. The frequent coexistence of co-morbid illness and psychosocial issues in older patients often makes diagnosis and management difficult, and prognostic parameters of elderly patients with CHF have not been definitely identified. Therefore, objective parameters are needed to diagnose and assess the severity of CHF in elderly patients.

A number of parameters are useful to predict prognosis of patients with CHF[13–17]. However, many modern markers are used only for research purposes and are not widely available in routine clinical practice. Several studies have recently shown that serum level of uric acid is a promising marker for prognosis in CHF patients[18,19]. In addition, hyperuricemia is related to impaired oxidative metabolism and vascular dysfunction in CHF[20, 21].

The present study tried to clarify the clinical characteristics and prognosis of elderly CHF patients in our institution, and to assess whether uric acid levels can effectively estimate prognosis in elderly ($\geq$ 70 years) CHF patients. Serum uric acid levels were measured at admission and the association with subsequent cardiac events was assessed in 247 consecutive patients hospitalized for chronic heart failure.

SUBJECTS AND METHODS

Study design

We prospectively studied 247 consecutive patients who had been admitted for the treatment of worsening chronic heart failure, or for diagnosis and pathophysiological investigations, or therapeutic evaluations of heart failure from April 1996 to February 2005. Informed consent was obtained from all patients before participation in this study, and the protocol was approved by the Human Investigations Committee of our institution.

The diagnosis of heart failure was based on a history of dyspnea and symptomatic exercise intolerance with signs of pulmonary congestion or peripheral edema, or documentation of left ventricular enlargement or dysfunction by chest radiography, echocardiography, or radionuclide ventriculography. Baseline characteristics of the patients are presented in **Table 1**. Definite hypertension was defined as self-reported hypertension and systolic blood pressure $>$ 140 mmHg or diastolic blood pressure $>$ 90 mmHg, or patients received antihypertensive treatment. A diagnosis of diabetes and hyperlipidemia were obtained from medical records or patient history.

Venous blood samples were obtained at admission, and two-dimensional echocardiography was performed by experts unaware of patient characteristics within 1 week after admission. Attending physicians were kept unaware of the results of the biochemical markers, and optimal medical therapy was performed independently based on measurements such as improvement in symptoms, physical examination findings, and pulmonary congestion on chest radiography[22,23].

End-points and follow-up

No patients were lost to follow-up (mean follow-up 451 $\pm$ 235 days, range 5 to 1,080 days) after admission to Yamagata University Hospital. Events were adjudicated using medical records, electrocardiograms, chest radiographs, autopsy reports, death certificates, and witness statements[24,25]. The endpoints, which were judged independently by researchers, were cardiac death, defined as death from worsening heart failure or sudden cardiac death, and worsening heart failure requiring readmission. Sudden cardiac death was defined as death without definite premonitory symptoms or signs and was established by the attending physician.

Statistical analysis

Results are presented as the mean $\pm$ SD value for continuous variables and as the percentage of total patients for categorical variables. The independent samples *t*-test and chi-square test or linear regression analysis were used for comparison of continuous and categorical variables, respectively. p values $<$ 0.05 were considered statistically significant. Cox proportional hazard analyses were performed to determine the independent predictor of cardiac events for the entire population.

Table 1 Clinical characteristics of 247 patients with chronic heart failure

	≥70 years old (n=123)	<70 years old (n=124)
Age (yr)	77±5*	57±11
Sex (male/female)	59/64	84/40
NYHA functional class (I/II/III/IV)	17/50/41/15*	43/49/29/3
Hypertension	67(54)*	53(43)
Diabetes mellitus	24(20)	33(27)
Hyperlipidemia	20(16)	29(23)
Current smoking	17(14)*	39(31)
Etiology of chronic heart failure		
Dilated cardiomyopathy	44(36)	46(37)
Ischemic heart disease	29(24)	33(27)
Valvular heart disease	26(21)	22(18)
Hypertensive heart disease	18(14)	10(8)
Tachycardia-induced cardiomyopathy	6(5)	13(10)
Blood examination at admission		
Uric acid (mg/dl)	6.35±2.26*	5.89±1.87
Creatinine (mg/dl)	0.91±0.31	0.88±0.30
Hemoglobin (g/dl)	12.6±1.98	13.7±2.12
Na (mEq/l)	140±3.5	141±2.7
Echocardiography at admission		
LVEDD (mm)	52±9.8	54±9.8
LVEF (%)	49±19	47±19
Cardiac events		
Cardiac deaths	18(15)*	6(5)
Re-hospitalizations	29(24)*	19(15)
Total events	47(38)*	25(20)
Medical treatment		
ACE inhibitors and/or ARBs	88(72)*	73(59)
Beta-blockers	38(31)	36(29)
Ca channel blockers	31(25)	30(24)
Spironolactone	31(25)	26(21)
Loop diuretics	79(64)*	54(44)
Digoxin	46(37)*	27(22)
Statins	15(12)	18(15)
Allopurinol	17(14)	15(12)

( ): %. *p<0.05 vs <70 years old group.
NYHA=New York Heart Association; LVEDD=left ventricular dimension at enddiastole; LVEF=left ventricular ejection fraction; ACE=angiotensin-converting enzyme; ARB=angiotensin II receptor blocker.

Independent predictors selected by univariate analysis were entered into multivariate analysis. We determined the multivariate-adjusted risk for quartiles 2 through 4 compared with quartile 1. Cardiac event-free curve was computed according to the Kaplan-Meier method and analyzed by a log-rank test. All analyses were performed using a standard statistical program package (StatView, version 5.0, SAS Institute Inc).

RESULTS

Clinical characteristics of elderly CHF patients

Comparison of the clinical characteristics between CHF patients aged ≥70 and <70 years is presented in **Table 1**. Elderly CHF patients ≥70 years had higher rate of hypertension, lower current smoking rate and higher uric acid levels than those aged <70 years. There were no differences in dia-

Table 2 Comparisons of clinical characteristics of 123 elderly patients with chronic heart failure between event-free and cardiac event groups

	Event-free (n=76)	Cardiac event (n=47)	p value
Age (yr)	78±5	77±5	0.5273
Sex (male/female)	32/44	27/20	0.2988
NYHA functional class (Ⅰ/Ⅱ/Ⅲ/Ⅳ)	14/36/21/5	3/14/20/10	0.0039
Hypertension	47(62)	20(43)	0.0369
Diabetes mellitus	15(20)	9(19)	0.9363
Hyperlipidemia	10(13)	10(21)	0.2358
Current smoking	8(11)	9(19)	0.1782
Etiology of chronic heart failure			
Ischemic heart disease	19(25)	10(21)	
Non-ischemic heart disease	57(75)	37(79)	0.1492
Blood examination at admission			
Uric acid (mg/dl)	5.9±2.0	6.8±2.6	0.0082
Creatinine (mg/dl)	0.84±0.24	0.97±0.37	0.0063
Hemoglobin (g/dl)	12.7±1.96	12.8±2.05	0.6322
Na (mEq/l)	141±2.5	140±4.5	0.2980
Echocardiography at admission			
LVEDD (mm)	51±9	53±11	0.3261
LVEF (%)	51±18	46±21	0.1913

( ): %.
Abbreviations as in Table 1.

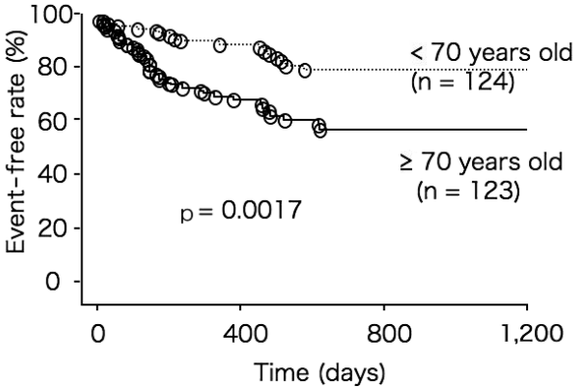

Fig. 1 Kaplan-Meier analysis of cardiac event-free rates in patients with chronic heart failure

betes mellitus, hyperlipidemia, etiologies of heart failure, serum creatinine levels, Na levels, hemoglobin levels, or echocardiographic findings. Elderly CHF patients aged ≥ 70 years were given angiotensin-converting enzyme inhibitors/angiotensin Ⅱ receptor blockers, loop diuretics and digoxin more frequently than those aged < 70 years.

The 247 CHF patients had 72 cardiac events during a mean follow-up period of 451 ± 235 days, and 47 of these 72 events (65%) occurred in those aged ≥ 70 years. Rates of cardiac death (15% vs 5%), re-hospitalization (23% vs 15%), and total cardiac events (38% vs 20%) were significantly higher in patients aged ≥ 70 years (**Table 1**). Kaplan-Meier analysis also showed that elderly CHF patients aged ≥ 70 years had significantly lower cardiac event-free rates (p = 0.0017; **Fig. 1**).

Clinical outcomes in elderly CHF patients

In 123 elderly patients with CHF, there were 12 non-cardiac deaths (3 cerebral hemorrhage, 3 colon cancer, 2 ileus, 2 pneumonia, and 2 suicides) and 47 cardiac events (38%), including 18 cardiac deaths (3 in-hospital deaths) and 29 readmissions for worsening heart failure. Thirty of the 47 cardiac events (64%) occurred within 12 months after admission (3 in-hospital cardiac deaths, 11 cardiac deaths, and 16 readmissions for worsening heart failure). The cause of cardiac death was worsening chronic heart failure in 11 patients, fatal acute myocardial infarction in 3 patients and sudden death in 4 patients. The 3 in-hospital cardiac deaths

Table 3 Univariate and multivariate analyses of predictors of cardiac events in elderly chronic heart failure patients

Variable	Hazard ratio	95% confidence interval	*p* value
Univariate analysis			
Uric acid	1.803	1.199−2.337	<0.0001
Creatinine	2.431	1.833−6.743	0.0107
NYHA functional class	1.935	1.227−2.587	0.0332
Multivariate analysis			
Uric acid	1.544	1.215−2.582	<0.0001
Creatinine	1.846	0.952−4.434	0.1110
NYHA functional class	1.250	0.873−3.772	0.3502

Abbreviation as in Table 1.

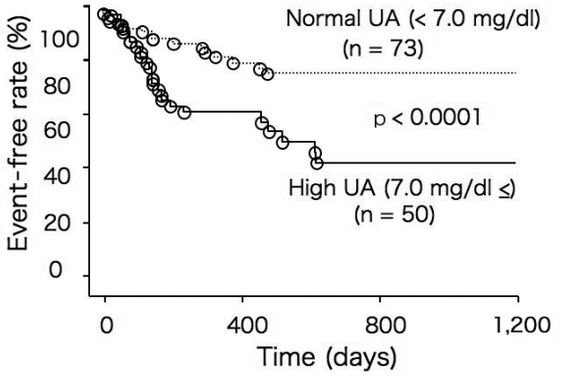

Fig. 2 Kaplan-Meier analysis of cardiac event-free rates in elderly patients with chronic heart failure
UA = uric acid.

were caused by worsening chronic heart failure.

Clinical characteristics in the 123 elderly patients with CHF were compared between patients with and without cardiac events (**Table 2**). Patients with cardiac events had more severe New York Heart Association (NYHA) functional class ($p = 0.0039$), higher levels of uric acid ($p = 0.0082$), higher levels of creatinine ($p = 0.0063$), and lower rate of hypertension ($p = 0.0369$) compared to those without cardiac events. Other parameters including age, sex, numbers of patients with ischemic heart disease, levels of hemoglobin and Na, and echocardiographic data were not significantly different. Medical treatments such as digitalis, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, statins, Ca channel blockers, β-blockers, and allopurinol at discharge were also similar in the two groups.

High uric acid levels (≥ 7.0 mg/d*l*) were observed in 2 of 17 patients (11.8%) with NYHA functional class I, in 19 of 50 patients (38.0%) with class II, in 20 of 41 patients (48.8%) with class III, and in 9 of 15 patients (60.0%) with class IV ($p = 0.0236$). Uric acid levels were not different between patients with ischemic and non-ischemic etiologies (5.9 ± 2.5 vs 6.4 ± 2.3 mg/d*l*, $p = 0.2662$). In patients with NYHA functional class III/IV, use of loop diuretics was more frequent compared to patients with NYHA class I / II [44/56 (78.6%) vs 35/67 (52.2%), $p = 0.0097$].

Comparison of uric acid levels and cardiac event rates between patients with preserved left ventricular systolic function (≥ 50%) and those with reduced left ventricular systolic function (< 50%) showed no significant difference.

Independent predictors of cardiac events in elderly CHF patients

Prognostic variables to predict cardiac events in elderly CHF patients were examined by univariate and multivariate Cox proportional hazard analyses (**Table 3**). Univariate analysis related uric acid, creatinine, and NYHA functional class to subsequent cardiac events. Thus, these three parameters were entered into multivariate analysis. Multivariate analysis showed uric acid was the only independent predictor of cardiac events in elderly patients with CHF [hazard ratio 1.544, 95% confidence interval (CI) 1.215−2.582, $p < 0.0001$].

Kaplan-Meier curves were constructed for patients with normal and high levels of uric acid (**Fig. 2**). Patients with high uric acid levels (≥ 7.0 mg/d*l*) had significantly lower cardiac event-

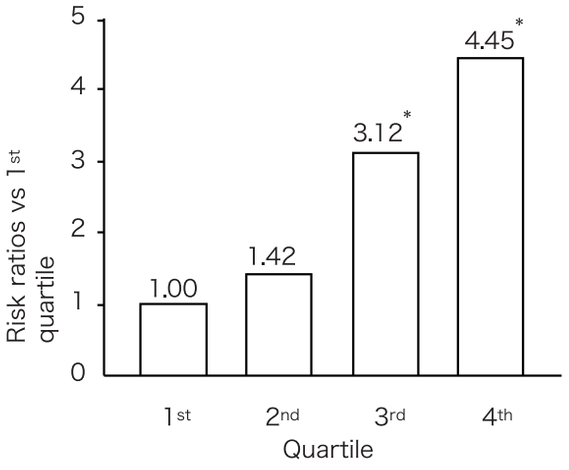

Fig. 3 Association between concentrations of serum uric acid and cardiac events in 123 elderly patients with chronic heart failure
Patients were divided into four groups based on the uric acid levels:1st quartile($\leq$5.0 mg/d*l*, $n=30$), 2nd quartile(5.1−6.4 mg/d*l*, $n=30$), 3rd quartile(6.5−8.6 mg/d*l*, $n=31$), and 4th quartile(8.7 mg/d*l*$\leq$, $n=32$). Hazard ratios relative to 1st quartile are shown.
*$p<0.05$ vs 1st quartile patients.

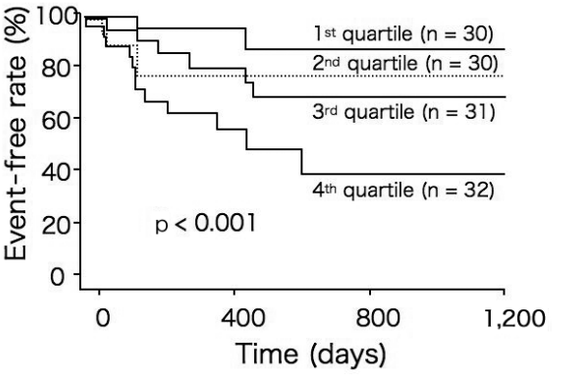

Fig. 4 Kaplan-Meier analysis of elderly patients with chronic heart failure
Patients divided into four groups as in Fig. 3.

free rates than those with normal uric acid levels (< 7.0 mg/d*l*). Serum uric acid levels could reliably risk stratify elderly patients with CHF for future cardiac events.

Graded relationships between uric acid levels and cardiac events

Patients were divided into four groups based on the uric acid levels: 1st quartile($\leq$5.0 mg/d*l*, $n=30$), 2nd quartile(5.1−6.4 mg/d*l*, $n=30$), 3rd quartile(6.5−8.6 mg/d*l*, $n=31$), and 4th quartile(8.7 mg/d*l*$\leq$, $n=32$). In the highest quartile, NYHA functional class was more severe, creatinine level was higher, and left ventricular ejection fraction was lower than in the lower three quartiles (**Table 4**). The highest quartile of uric acid was associated with the highest risk of cardiac events (4.45-fold compared to the lowest quartile)as shown in **Fig. 3**. Hazard ratios were 1.000, 1.424 (95% CI 0.479−2.254), 3.118(CI 1.011−6.181), and 4.453(CI 1.201−8.889)for quartiles 1 through 4. Cumulative event-free curves were constructed by the Kaplan-Meier method(**Fig. 4**). Patients in the highest quartile had a significantly lower cardiac event-free rate than the other three quartiles ($p<0.001$).

DISCUSSION

Our results demonstrated that serum uric acid level was associated with a high risk of cardiac events in elderly patients with CHF. Uric acid level could potentially improve the risk stratification of elderly with CHF.

It is important to accurately define prognostic factors in patients with heart failure to identify high-risk individuals who require closer follow-up and more intensive intervention. A number of parameters can predict the prognosis of patients with CHF[13−17]. Brain natriuretic peptide is released from the ventricles as ventricular function deteriorates, and is a well-established prognostic indicator in CHF patients[14,26]. However, many modern parameters are used only for research purposes and are not widely available. Therefore, simple markers that can be measured anywhere at low cost are necessary. High serum uric acid levels are a strong, independent marker of impaired prognosis in patients with moderate and severe heart failure[18,19]. Hyperuricemia is a marker of impaired oxidative metabolism, hyperinsulinemia, inflammatory cytokine activation, and vascular dysfunction[20,21]. In the present study, we examined the potential prognostic value of uric aid in elderly persons with CHF. Univariate and multivariate Cox proportional hazard analyses demonstrated that uric acid level was an independent predictor of future cardiac events(**Table 3**). We also showed that the risk of cardiac events increased with increasing uric acid level. The highest quartile of uric acid level was associated with a 4.45-fold event risk(**Fig. 3**).

In the present study, elderly CHF patients

Table 4 Comparisons of clinical characteristics in elderly chronic heart failure patients between quartiles of uric acid levels

	1st quartile (n=30)	2nd quartile (n=30)	3rd quartile (n=31)	4th quartile (n=32)
Uric acid range (mg/d*l*)	≤5.0	5.1−6.4	6.5−8.6	8.7≤
Age (yr)	77±6	77±5	77±6	79±5$^{\#}$
Sex (male/female)	16/14	14/16	12/19	17/15
NYHA functional class	2.0±0.7	2.2±0.9	2.4±0.7*	2.9±0.6**$^{\#}$
Hypertension	22(73)	15(50)	17(55)	13(41)
Diabetes mellitus	8(27)	4(13)	5(16)	7(22)
Hyperlipidemia	7(23)	5(17)	5(16)	3(9)
Current smoking	6(20)	3(10)	4(13)	4(13)
Etiology of chronic heart failure				
Dilated cardiomyopathy	7(23)	14(47)	11(35)	12(38)
Ischemic heart disease	8(27)	5(17)	8(26)	8(25)
Valvular heart disease	5(17)	7(23)	6(19)	8(25)
Hypertensive heart disease	8(27)	1(3)	5(16)	4(13)
Tachycardia-induced Cardiomyopathy	2(7)	3(10)	1(3)	0
Blood examination				
Uric acid (mg/d*l*)	4.0±0.8	5.7±0.4**	7.6±0.7**$^{\#\#}$	9.4±2.1**$^{\#\#}$
Creatinine (mg/d*l*)	0.78±0.24	0.88±0.20	0.98±0.29*	1.03±0.39*
Hemoglobin (g/d*l*)	12.2±2.1	13.1±1.9	12.6±1.8	12.3±2.1
Na (mEq/*l*)	141±4.4	141±2.4	141±3.5	140±3.4
Echocardiography				
LVEDD (mm)	49±10	53±9	52±10	53±11
LVEF (%)	60±19	51±14	48±21*	40±18**$^{\#}$
Cardiac events				
Cardiac deaths	5(17)	4(13)	3(10)	6(19)
Re-hospitalizations	1(3)	6(20)	10(32)	12(38) †
Total events	6(20)	10(33)	13(42)	18(56) †
Treatment before admission				
ACE inhibitors and/or ARBs	22(73)	17(57)	27(87)	22(69)
Beta-blockers	5(17)	9(30)	12(39)	12(38)
Ca channel blockers	12(40)	7(23)	9(29)	3(9)
Spironolactone	5(17)	10(33)	7(23)	9(28)
Loop diuretics	13(43)	20(67)	21(68)	25(78) †
Digoxin	6(20)	15(50)	10(32)	15(47)
Statins	4(13)	5(17)	3(10)	3(9)
Allopurinol	3(10)	5(17)	2(6)	7(22)

( ): %.*$p<0.05$ vs 1st quartile, $^{\#}p<0.05$ vs 2nd quartile, and $p<0.05$ vs 3rd quartile.**$p<0.01$ vs 1st quartile, $^{\#\#}p<0.01$ vs 2nd quartile, and $p<0.01$ vs 3rd quartile. †$p<0.05$ by chi-square test.

aged ≥ 70 years had higher uric acid levels than those aged < 70 years, suggesting decreases in renal function with aging. In addition, elderly CHF patients aged ≥ 70 years were given loop diuretics more frequently than those aged < 70 years, and this might affect the higher uric acid levels in the elderly.

The incidence and prevalence of CHF increase dramatically with advancing age[1−5]. Increasing age has been reported to increase the mortality of CHF patients[8−12]. However, prognostic assessment of elderly patients with CHF is far from clearly estab-

lished. Epidemiologic data indicate that CHF represents a crucial problem in the elderly population in terms of social, economic, and health burden[8–12]. Despite their importance in the worsening of CHF and prevention of the progression of this syndrome, the risks of re-hospitalization and the causes of exacerbation have not been systematically evaluated. In addition, the detailed mechanisms behind the increased mortality in older CHF patients are still unclear[6,7]. In the present study, we examined the clinical characteristics and the potential prognostic value of uric aid in elderly CHF patients aged ≥ 70 years, because the prevalence of CHF increases[1] and these patients have higher rate of readmission and mortality[27,28]. Ageing is associated with important structural and functional changes in the vascular system and the heart, but little is known about how ageing interacts with the pathophysiology underlying the process of developing heart failure. Further research needs to elucidate more effective treatment strategies for prevention of CHF and to decrease the morbidity and mortality of CHF in the elderly.

CONCLUSIONS

These data suggest that high serum uric acid level is a reliable marker for prognosis in the elderly patients with chronic heart failure. We suggest that measurement of uric acid levels should be considered as a routine measurement in the assessment and follow-up for elderly patients with chronic heart failure with low cost and wide availability.

Acknowledgments

This study was supported in part by a grant-in-aid for Scientific Research (No. 17590702) from the Ministry of Education, Science, Sports and Culture, Japan and grants from The Japan Heart Foundation, The Mochida Memorial Foundation, and Takeda Science Foundation.

要　　約

高齢者心不全高尿酸血症は心事故率の高さと相関する

新関　武史　竹石　恭知　有本　貴範　奥山　英伸　野崎　直樹
廣野　摂　角田　裕一　渡辺　哲　二藤部丈治　宮下　武彦
高橋　大　小山　容　久保田　功

目　的: 心不全は高齢者の死亡と入院の主たる原因の一つである．リスクの高い高齢者心不全例の判別に役立つ指標の確立が求められている．尿酸値が心不全の予後予測に有用であると報告されているが，高齢者においてはまだ十分に検討されていない．本研究では当院の70歳以上の高齢者心不全症例の臨床的特徴を明らかにすること，高齢者心不全症例における尿酸値の予後予測としての有用性を検討することを目的とした．

方　法: 心不全の診断と治療のために入院した247例において，70歳以上の高齢者（123例）の臨床像を70歳未満の症例（124例）と比較した．入院時に採血し尿酸値を測定し，心血管事故の発生について平均451±235日間の追跡調査を行った．

結　果: 70歳以上の高齢者では70歳未満と比べて高血圧の合併が多く，喫煙率は低く，尿酸値は高値であった．観察期間中，心血管死と心不全増悪による再入院を含む72件の心事故が発生した．心事故群で尿酸値は高値で，Cox比例ハザード解析では尿酸値は予後を予測する独立した危険因子であった（ハザード比1.544, 95%信頼区間1.215－2.582, $p < 0.0001$）．尿酸値が高いほど相対的リスクは高く，Kaplan-Meier 解析でも尿酸値は高齢者心不全のリスクの判別に有用であることが示された．

結　語: 尿酸値は簡便に低コストで測定でき，高齢者心不全例の予後予測に有用であった．

J Cardiol 2006 May; 47(5): 219−228

References

1) Senni M, Tribouilloy CM, Rodeheffer RJ, Jacobsen SJ, Evans JM, Bailey KR, Redfield MM: Congestive heart failure in the community: A study of all incident cases in Olmsted County, Minnesota, in 1991. Circulation 1998; **98**: 2282−2289
2) Mosterd A, Hoes AW, de Bruyne MC, Deckers JW, Linker DT, Hofman A, Grobbee DE: Prevalence of heart failure and left ventricular dysfunction in the general population: The Rotterdam Study. Eur Heart J 1999; **20**: 447−455
3) Senni M, Tribouilloy CM, Rodeheffer RJ, Jacobsen SJ, Evans JM, Bailey KR, Redfield MM: Congestive heart failure in the community: Trends in incidence and survival in a 10-year period. Arch Intern Med 1999; **159**: 29−34
4) Cohen-Solal A, Desnos M, Delahaye F, Emeriau JP, Hanania G: A national survey of heart failure in French hospitals: The Myocardiopathy and Heart Failure Working Group of the French Society of Cardiology, the National College of General Hospital Cardiologists and the French Geriatrics Society. Eur Heart J 2000; **21**: 763−769
5) Davies MK, Hobbs FDR, Davis RC, Kenkre JE, Roalfe AK, Hare R, Wosornu D, Lancashire RJ: Prevalence of left-ventricular systolic dysfunction and heart failure in the Echocardiographic Heart of England Screening study: A population based study. Lancet 2001; **358**: 439−444
6) Rich MW: Management of heart failure in the elderly. Heart Fail Rev 2002; **7**: 89−97
7) Sharma R, Coats AJS, Anker SD: The role of inflammatory mediators in chronic heart failure: Cytokines, nitric oxide, and endothelin-1. Int J Cardiol 2000; **72**: 175−186
8) Schocken DD, Arrieta MI, Leaverton PE, Ross EA: Prevalence and mortality rate of congestive heart failure in the United States. J Am Coll Cardiol 1992; **20**: 301−306
9) Bourassa MG, Gurne O, Bangdiwala SI, Ghali JK, Young JB, Rousseau M, Johnstone DE, Yusuf S: Natural history and patterns of current practice in heart failure: The Studies of Left Ventricular Dysfunction (SOLVD) Investigators. J Am Coll Cardiol 1993; **22**(Suppl A): 14A−19A
10) McDermott MM, Feinglass J, Lee PI, Mehta S, Schmitt B, Lefevre F, Gheorghiade M: Systolic function, readmission rates, and survival among consecutively hospitalized patients with congestive heart failure. Am Heart J 1997; **134**: 728−736
11) MacIntyre K, Capewell S, Stewart S, Chalmers JW, Boyd J, Finlayson A, Redpath A, Pell JP, McMurray JJ: Evidence of improving prognosis in heart failure: Trends in case fatality in 66547 patients hospitalized between 1986 and 1995. Circulation 2000; **102**: 1126−1131
12) Cowie MR, Wood DA, Coats AJ, Thompson SG, Suresh V, Poole-Wilson PA, Sutton GC: Survival of patients with a new diagnosis of heart failure: A population based study. Heart 2000; **83**: 505−510
13) Bettencourt P, Ferreira A, Dias P, Pimenta J, Frioes F, Martins L, Cerqueria-Gomes M: Predictors of prognosis in patients with stable mild to moderate heart failure. J Card Fail 2000; **6**: 306−313
14) Maeda K, Tsutamoto T, Wada A, Mabuchi N, Hayashi M, Tsutsui T, Ohnishi M, Sawaki M, Fujii M, Matsumoto T, Kinoshita M: High levels of plasma brain natriuretic peptide and interleukin-6 after optimized treatment for heart failure are independent risk factors for morbidity and mortality in patients with congestive heart failure. J Am Coll Cardiol 2000; **36**: 1587−1593
15) Setsuta K, Seino Y, Ogawa T, Arao M, Miyatake Y, Takano T: Use of cytosolic and myofibril markers in the detection of ongoing myocardial damage in patients with chronic heart failure. Am J Med 2002; **113**: 717−722
16) Goto T, Takase H, Toriyama T, Sugiura T, Sato K, Ueda R, Dohi Y: Circulating concentrations of cardiac proteins indicate the severity of congestive heart failure. Heart 2003; **89**: 1303−1307
17) Brophy JM, Dagenais GR, McSherry F, Williford W, Yusuf S: A multivariate model for predicting mortality in patients with heart failure and systolic dysfunction. Am J Med 2004; **116**: 300−304
18) Leyva F, Anker SD, Godsland IF, Teixeira M, Hellewell G, Kox WJ, Poole-Wilson PA, Coats AJ: Uric acid in chronic heart failure: A marker of chronic inflammation. Eur Heart J 1998; **19**: 1814−1822
19) Anker SD, Doehner W, Rauchhaus M, Sharma R, Francis D, Knosalla C, Davos CH, Cicoira M, Shamim W, Kemp M, Segal R, Osterziel KJ, Leyva F, Hetzer R, Ponikowski P, Coats AJ: Uric acid and survival in chronic heart failure: Validation and application in metabolic, functional, and hemodynamic staging. Circulation 2003; **107**: 1991−1997
20) Hoeper MM, Hohlfeld JM, Fabel H: Hyperuricaemia in patients with right or left heart failure. Eur Respir J 1999; **13**: 682−685
21) Alderman MH: Uric acid and cardiovascular risk. Curr Opin Pharmacol 2002; **2**: 126−130
22) Committee on Evaluation and Management of Heart Failure: Guidelines for the evaluation and management of heart failure: Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 1995; **92**: 2764−2784
23) Arimoto T, Takeishi Y, Shiga R, Fukui A, Tachibana H, Nozaki N, Hirono O, Nitobe J, Miyamoto T, Hoit BD, Kubota I: Prognostic value of elevated circulating heart-type fatty acid binding protein in patients with congestive heart failure. J Card Fail 2005; **11**: 56−60
24) Packer M, O'Connor CM, Ghali JK, Pressler ML, Carson PE, Belkin RN, Miller AB, Neuberg GW, Frid D, Wertheimer JH, Cropp AB, DeMets DL, for the Prospevtive Randomized Amlodipine Survial Evaluation Study Group: Effect of amlodipine on morbidity and mortality in severe chronic heart failure. N Engl J Med 1996; **335**: 1107−1114
25) O'Connor CM, Carson PE, Miller AB, Pressler ML, Belkin RN, Neuberg GW, Frid DJ, Cropp AB, Anderson S, Wertheimer JH, DeMets DL: Effect of amlodipine on mode of death among patients with advanced heart failure in the PRAISE trial: Prospective Randomized Amlodipine Survival Evaluation. Am J Cardiol 1998; **82**: 881−887
26) Bettencourt P, Ferreira A, Dias P, Pimenta J, Frioes F, Martins L, Cerqueria-Gomes M: Predictors of prognosis in patients with stable mild to moderate heart failure. J Card Fail 2000; **6**: 306−313
27) Rich MW, Freedland KE: Effect of DRGs on three-month readmission rate of geriatric patients with congestive heart

failure. Am J Public Health 1988; **78**: 680−682
28) Vinson JM, Rich MW, Sperry JC, Shah AS, McNamara T: Early readmission of elderly patients with congestive heart failure. J Am Geriatr Soc 1990; **38**: 1290−1295